

### Remarks

Paper No. 11 presented rejections of the claims of the present application under: (a) 35 U.S.C. §112, first paragraph; (b) 35 U.S.C. §112, second paragraph; and (c) 35 U.S.C. §103(a). Each of these rejections is addressed below.

#### I. 35 U.S.C. §112, First Paragraph

Claims 5-13 were rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, has possession of the claimed invention. Independent claims 5 and 8 have been amended so as to convey the invention described at page 6, line 25 through page 7, line 1, where it is taught that the reduction of surface tension of a liquid enhances the effects of the application of ultrasonic energy.

#### II. 35 U.S.C. §112, Second Paragraph

Claims 5-13 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It was specifically alleged that the recitations of "the standard state surface tension of said second liquid is reduced" and "the standard state surface tension of said first liquid is reduced" lack antecedent basis.

Independent claims 5 and 8 have been amended so as to correct the alleged lack of antecedent basis.

#### III. 35 U.S.C. §103(a)

Claims 1 and 3-13 were rejected under 35 U.S.C. §103(a) as being unpatentable over Buck et al. in view of Robson et al. and Robbins et al.

##### A. Buck et al.

Applicants' interpretation of Buck et al. was questioned. It is respectfully submitted that Applicants' interpretation of Buck et al. is correct, and that this correct interpretation of Buck et al. does not suggest the claimed invention to one of ordinary skill in the art.

The sonication method of Buck et al. ("method iv") only refers to method iii for a centrifugation technique. Specifically, the description of method iv states that "[t]he suspensions were centrifuged as described above for method iii, ...." The description of method iii states that "[s]uspensions were centrifuged at 16,000 x g for 5 min, and the fluid poured off."

At this point method iv and method iii diverge. In method iv, the centrifuged suspensions are "washed twice with distilled water, and then resuspended in the residual water (approximately 25 ul)" (emphasis added). In contrast, in method iii, "[f]ifty microliters of either

distilled water or 2% Triton X-100 in PCR buffer” is added to the centrifuged suspensions. The assertion in Paper No. 11 that “it would have been a matter of choice for one of skill in the art to use either distilled water and/or PCR buffer” as the liquid in which cells are sonicated is not supportable. In its sonication method, Buck et al. teaches only the use of distilled water and there is no suggestion that PCR buffer would be a suitable alternative to water.

Furthermore, Buck et al. fails to teach one skilled in the art of the enhancement of a sonication cell disruption method by alkalization of this sonication solution. The use of PCR buffer in methods i, ii and iii of Buck et al. are not critical to cell disruption. Rather, the use of PCR buffer in each of these methods serves only to secure optimal pH conditions for *Taq* DNA polymerase enzyme.

Moreover, the manner of sonication described by Buck et al. is fundamentally different from the claimed method. Specifically, the claimed method uses a sonic bath. In contrast, Buck et al. teaches that “tubes were placed in a plastic rack that was floated in a dish of water next to the sonicator probe (Sonics & Materials, Danbury, Conn.) and sonicated at 45 W.” The disadvantages and disincentives of using a sonicator probe are discussed in the present application at page 2, lines 9-25. These disadvantages and disincentives are further evidenced by Murphy et al. (U.S. 5,374,522) which describes the significant differences between a probe sonic oscillator (sonic probe of Buck et al.) and a sonic bath (see column 9, line 48-column 10, line 12). Due to these significant differences, it is respectfully submitted that one of ordinary skill in the art would not be led to use a sonic bath without beads for the lysis of cells from the teaching of Buck et al. which describes a significantly different and inferior method using a sonic probe.

B. Robson et al.

With regard to Robson et al., column 6, lines 26-40 was cited as providing a teaching that mycobacterial cells to be disrupted may be in water or alkalized solutions. However, as with Buck et al., Robson et al. does not teach one skilled in the art that alkalization of a solution enhances a sonication cell disruption method. Column 6, lines 26-40 is a mere laundry list of acceptable mileaus in which mycobacterial cells may be heated. In every working Example of Robson et al. that utilizes sonication, the sonication solution is water. Specifically, Examples 2, 4 and 5 are directed to sonication methods, and in all these Examples, the samples were diluted or reconstituted in water.

The teaching of Robson et al. is directed to that which is claimed; a process for lysis of Mycobacteriaceae by exposure to heat in the absence of other lysogenic agents and other lysogenic conditions. Thus, Robson et al. is not teaching one skilled in the art of the enhancement of cell disruption by alkalizing a sonication solution.

C. Robbins et al.

With regard to Robbins et al., column 3, lines 19-23 was cited as providing a teaching of the application of an alkaline pH for preparation of the cells before sonication to cause disruption of the cells. However, as with Buck et al. and Robson et al., Robbins et al. also does not teach one skilled in the art that alkalization of a solution aids cell disruption using sonication. Column 3, lines 19-23 states that "dilute alkali may be incorporated in the wash to remove adhering color and taste bodies" (emphasis added). There is no teaching of the nature or pH of the sonication solution in Robbins et al.

D. Summary

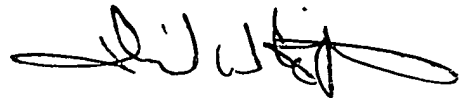
In summary, it is respectfully submitted that there are significant differences between the invention claimed in the present application and the teachings of the cited references. It is also respectfully submitted that the teachings of the cited references fail to provide sufficient suggestion or motivation for those skilled in the art to address these significant differences to arrive at the claimed invention.

Specifically, the suggestion or motivation to alkalize a sonication solution to enhance cell disruption is lacking, because, to the extent the cited references utilize alkaline solutions, there is no recognition of its utility in a sonication based cell disruption method. Thus, it is respectfully submitted that one skilled in the art would not combine the fragmented teachings of the cited references to yield the claimed invention, but for the Applicants' teachings in the present application.

IV. Conclusions

In view of the claim amendments and remarks above, the present application is now believed to be in condition for allowance.

Respectfully submitted,



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